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Human Genome Epidemiology (HuGE) Review

XRCC3 and *XPD*/*ERCC2* Single Nucleotide Polymorphisms and the Risk of Cancer: A HuGE Review

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Hundreds of polymorphisms in DNA repair genes have been identified; however, for many of these polymorphisms, the impact on repair phenotype and cancer susceptibility remains uncertain. In this review, the authors focused on the x-ray repair cross-complementing protein group 3 (*XRCC3*) and xeroderma pigmentosum group D (*XPD*)/excision repair cross-complementing rodent repair deficiency (*ERCC2*) genes, because they are among the most extensively studied but no final conclusion has yet been drawn about their role in cancer occurrence. XRCC3 participates in DNA double-strand break/recombinational repair through homologous recombination to maintain chromosome stability. XPD/ERCC2 is a helicase involved in the nucleotide excision repair pathway, which recognizes and repairs many structurally unrelated lesions, such as bulky adducts and thymidine dimers. The authors identified a sufficient number of epidemiologic studies on cancer to perform meta-analyses for *XPD*/*ERCC2* variants in codons 156, 312, and 751 and *XRCC3* variants in codon 241. The authors evaluated all cancer sites to investigate whether DNA repair is likely to take place in a rather nonspecific manner for different carcinogens and different cancers. For the most part, the authors found no association between these genes and the cancer sites investigated, except for some statistically significant associations between *XPD*/*ERCC2* single nucleotide polymorphisms and skin, breast, and lung cancers.

ERCC2; ERCC2 protein, human; genetics; meta-analysis; neoplasms; *XPD*; *XRCC3*; x-ray repair cross complementing protein 3

Abbreviations: *ERCC*, excision repair cross-complementing rodent repair deficiency; HuGE, Human Genome Epidemiology; SNP, single nucleotide polymorphism; *XPD*, xeroderma pigmentosum group D; *XRCC*, x-ray repair cross-complementing protein.

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GENE(S)

DNA repair genes are involved in rare and cancer-inducing conditions such as xeroderma pigmentosum (a genetic

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condition in which even short exposure to ultraviolet light can lead to early death from cancer). These genes also show common polymorphisms, whose effects on DNA repair enzymes are milder. A number of studies suggest that such mild defects in DNA repair may predispose to cancer (1–3). Environmental and occupational chemical carcinogens, such as polycyclic aromatic hydrocarbons, aromatic amines, and *N*-nitroso compounds, form bulky DNA adducts that are repaired mostly through the nucleotide excision repair pathway (e.g., the xeroderma pigmentosum group D (*XPD*) gene, also called the excision repair cross-complementing rodent repair deficiency group 2 (*ERCC2*) gene). These agents can also produce interstrand cross-links that are repaired by genes involved in both nucleotide excision repair pathways (e.g., the excision repair cross-complementing rodent repair deficiency group 1 (*ERCC1*) and group 4 (*ERCC4*) genes) and homologous recombinational repair pathways (e.g., x-ray repair cross-complementing protein group 2 or 3 (*XRCC2-3*)). Reactive oxygen species also can induce base damage, abasic sites, single strand breaks, and double strand breaks. Single strand breaks are repaired through the base excision repair pathway (e.g., x-ray repair cross-complementing protein group 1 (*XRCC1*), proliferating cell nuclear antigen (*PCNA*)), while double strand breaks are corrected by either homologous recombination (e.g., *XRCC2-3*) or nonhomologous end-joining pathways. Hundreds of polymorphisms in DNA repair genes have been identified; however, for many of these polymorphisms, the impact on repair phenotype and cancer susceptibility remains uncertain (1, 3).

Among the different DNA repair pathways, we focused in this Human Genome Epidemiology (HuGE) review on *XRCC3* and *XPD* because, besides the genes already discussed by Hung et al. (4) in a recent HuGE review, these genes are among the most extensively studied for their potential implication in cancer risk. Although *XPD* and *XRCC3* belong to two different repair pathways (nucleotide excision repair and homologous recombination, respectively), there is evidence that for some important exposures (e.g., smoking), both genes could be involved in repairing the relevant DNA damage (5). However, no final conclusion has yet been drawn about their role in cancer occurrence.

The *XRCC3* gene is located in the 14q32.3 region. The XRCC3 protein participates in DNA double-strand break/recombinational repair and is a member of a family of Rad-51-related proteins that probably participate in homologous recombination to maintain chromosome stability and repair DNA damage (6). *XPD* is located at chromosome 19q13.3 and is involved in the nucleotide excision repair pathway, which recognizes and repairs many structurally unrelated lesions, such as bulky adducts and thymidine dimers (7). *XPD* functions as an adenosine triphosphate-dependent 5′-3′-helicase joint to the basal transcription factor IIH complex. Its protein has a role in the initiation of RNA transcription by RNA polymerase II (8).

No meta-analysis of data on the *XRCC3* gene has been published, whereas for *XPD*, only lung cancer risk has been evaluated by meta-analysis (9, 10).

GENE VARIANTS

For the *XPD* gene, eight coding single nucleotide polymorphisms (SNPs) (four synonymous and four amino acid substitutions) and 138 intronic SNPs have so far been included in the National Center for Biotechnology Information's SNP database (http://www.ncbi.nlm.nih.gov/projects/SNP/). For the *XRCC3* gene, four coding SNPs (one synonymous and three amino acid substitutions) and 109 intronic SNPs have been described, but most of them have not been studied in relation to cancer risk and thus were not considered in this review. We identified a sufficient number of epidemiologic studies on cancer to perform meta-analyses only for the *XPD* variants Arg156Arg (C/A), Asp312Asn (G/A), and Lys751Gln (A/C) and for the *XRCC3* variant Thr241Met (C/T). Sparse data are available for *XPD*-Asp711Asp (C/T), -His201Tyr (C/T), -Ile199Met (C/G), and -IVS4-A/G and for *XRCC3*-IVS6 1571, -5′-UTR 4541, -A4552C, and -IVS5-14; those polymorphisms were not considered in this review. Allele and genotype frequencies for all of the polymorphisms are reported in Web table 1 (posted on the *Journal*'s website (http://www.aje.oxfordjournals.org)) by study and ethnicity. Genotype frequencies among controls were in agreement with those predicted under Hardy-Weinberg equilibrium in almost all populations (Web table 1).

GENOTYPE-PHENOTYPE CORRELATIONS

A variety of studies have been conducted to investigate the functional effects of variant DNA repair genes through the use of various biomarkers (3). However, these biomarker investigations did not provide consistent observations on genotype-phenotype correlations. This is probably due to the small sample sizes used and inappropriate biomarkers investigated, such as sister chromatid exchanges, because the mechanisms for formation of such changes and their biologic significance are unknown. Below we summarize the evidence on the relation between the *XRCC3* and *XPD*/*ERCC2* genotypes and the functional biomarkers that have been investigated to date (3, 11–16).

XRCC3

Allele and genotype frequencies of *XRCC3* polymorphisms considered in the present study are shown by ethnic group in Web table 1. Variant allele frequencies ranged from 5 percent to 45 percent, with a statistically significant difference in the prevalence of the *XRCC3*-241 polymorphism between different ethnic groups (the prevalence of Met/Met homozygosity was 4.6 percent in African Americans, 0.2 percent in Asians, and 12.4 percent in Caucasians; $p < 0.001$). An opposite allele frequency distribution was observed for the *XRCC3*-5′-UTR 4541 polymorphism in the study by Winsey et al. (17) as compared with other studies, indicating a possible inversion in the assignment of the alleles (Web table 1).

The *XRCC3*-241Met variation is a nonconservative change, but it does not reside in the adenosine triphosphate-binding domain, the only functional domain identified in the protein. The impact of this polymorphism on repair phenotype was studied in 80 healthy subjects (18); the *XRCC3* 241Met allele was associated with significant increases in chromosome deletions in x-ray-challenged blood lymphocytes ($p = 0.05$). Chromosome deletion is specific for abnormal repair of x-ray-induced DNA strand breakage. The overall frequency of aberrant cells associated with the variant was nonsignificantly higher than that in the wild-type genotype. On the other hand, the variant genotype had no effect on the repair of ultraviolet light-induced DNA damage in comparison with the wild-type genotype. These results suggest that the *XRCC3* 241Met allele might be defective in repairing double strand breaks but not in nucleotide excision repair.

In a study of 133 nonsmokers, 93 former smokers, and 82 current smokers, the *XRCC3* 241Met variant was significantly associated with increased bulky DNA adduct levels among all volunteers as a group and among the nonsmokers (14).

In blood samples taken from 435 newborns, the variant gene was not associated with an increase in the frequency of glycophorin A NN or NO mutations (16).

In the one study that investigated the *XRCC3*-241Met variant using a specific functional assay (19), the findings suggested that the increased cancer risk associated with the *XRCC3*-241 variant may not be attributable to an intrinsic homology-directed repair. However, such experiments cannot definitely rule out the involvement of other *XRCC3* variants in linkage disequilibrium or possible genetic interactions between the *XRCC3*-241 variant and polymorphic alleles of other DNA repair genes that may lead to a homology-directed repair defect. It is still possible that an extremely mild homology-directed repair defect would not be detectable in the assay or that *XRCC3* acts within other cellular pathways not assayed in this in vitro model.

XPD/ERCC2

A number of SNPs in the *XPD* gene have been reported. Among these SNPs, common polymorphisms have been observed at codons 312 and 751, with allelic frequencies ranging from 6 percent to 34 percent and from 9 percent to 37 percent, respectively. A statistically significant difference between different ethnic groups has been observed for *XPD/ERCC2*-751 (the prevalence of Gln/Gln homozygosity was 6.9 percent in African Americans, 1.1 percent in Asians, and 13.4 percent in Caucasians; $p < 0.001$) and *XPD/ERCC2*-312 (Asn/Asn homozygosity was absent in Asians and prevalence was 11.1 percent in Caucasians; $p < 0.001$) (Web table 1). The pattern of allele and genotype frequencies was very different in the study by Chen et al. (20) as compared with the other Asian populations, with approximately 18 percent of subjects carrying the homozygous Gln/Gln genotype. This could have been due to errors in genotyping, since it seems unlikely that such great variation would exist in a population where all persons were of the same ethnicity.

The above polymorphisms result, respectively, in amino acid changes of aspartic acid to asparagine (Asp/Asn) in codon 312 and lysine to glutamine (Lys/Gln) in codon 751. Studies of the functional significance of these *XPD* variants include studies of chromosome aberrations, p53 mutations, changes in DNA repair capacity, and formation of DNA adducts. Expression of induced chromosome damage in relation to polymorphisms in *XPD* codon 312 was investigated by Lunn et al. (13), Au et al. (18), and Gao et al. (12). Lunn et al. (13) studied blood samples from 31 female donors who had various risk factors for breast cancer. Lymphocytes were irradiated with x-rays, allowed to repair the damage for 1.5 hours, and then harvested for analyses of chromatid-type aberrations. No association between the variant genotype and aberrations was observed, supporting the suggestion that the *XPD* gene is not commonly involved in base excision repair, the primary repair pathway for damage induced by x-rays. In contrast, in another cytogenetic study, Au et al. (18) showed that *XPD* 312Asn is associated with defective repair of ultraviolet light-induced DNA damage. The observed damage consisted of chromatid-type aberrations that are derived specifically from insufficient repair of ultraviolet-induced DNA damage, that is, nucleotide excision repair deficiency. Consistent with the study by Lunn et al. (13), the variant genotype had no significant effect on chromosome damage following exposure to x-rays, again confirming that the variant genotype is not involved in base excision repair.

The cytogenetic observation, however, is different from the p53 gene mutation data from Gao et al. (12) among lung cancer patients. In that study, the wild-type *XPD* codon 312 Asp allele was significantly associated with the presence of mutations in p53 exons 5–8. This observation by Gao et al. (12) may have been influenced by the small number of patients with the p53 gene mutation ($n = 40$) and/or the low frequency of the mutation among lung cancer patients (20 percent) in that study population. The function of the *XPD* codon 751 polymorphism has been extensively investigated, but again the suitability of the biomarker for *XPD* can be brought into question in some of the studies. In a study of 308 healthy people by Matullo et al. (14), the variant 751Gln genotype was not associated with a significant increase in bulky DNA adducts. In addition, it was not correlated with sister chromatid exchange frequencies or with polyphenol DNA adducts among 76 normal volunteers (11). The lack of association may indicate that sister chromatid exchange and polyphenol DNA adducts are not relevant biomarkers for *XPD* variant genotypes in the nucleotide excision repair pathway.

In the study of 31 subjects mentioned above, Lunn et al. (13) reported that having the wild-type *XPD* codon 751 genotype was associated with a significant increase in x-ray-induced chromosome aberrations compared with the variant genotypes. However, the significant association was with the combined chromatid breaks and gaps, not with breaks alone. In addition, the *XPD* gene may not be involved in the repair of x-ray-induced damage that appears to predominantly require the base excision repair mechanism.

Data from a study conducted by Qiao et al. (15) indicated that post-ultraviolet defective repair capacity for nucleotide excision repair using the host cell reactivation assay can be modulated by genetic polymorphisms of *XPD* in healthy subjects. The homozygous forms of two *XPD* variant alleles, *XPD* 312Asn and *XPD* 751Gln, were associated with lower defective repair capacity of ultraviolet-induced DNA damage than were homozygous wild-type alleles. However, these effects were not statistically significant, possibly because of the inherently high variation in the host cell reactivation assay. In addition, cigarette smoking may have some confounding effects on the defective repair capacity.

In summary, *XPD* 312Asn and *XPD* 751Gln are deficient in the repair of ultraviolet-light-induced but not x-ray-induced chromosome aberrations, which probably reflects their involvement in nucleotide excision repair (3, 8, 11–13, 18). No data from biomarkers or functional in vitro studies are available for the *XPD* Arg156Arg polymorphism. Although no effect would be expected, since the amino acid does not change, linkage disequilibrium with a functional variant cannot be excluded. A further description of the *XPD* gene variants and their possible implications can be found in the paper by Benhamou and Sarasin (9).

DISEASES

DNA repair affects multiple diseases, particularly different types of cancer. Therefore, we included in the present meta-analyses studies that considered any type of cancer as the outcome. *XPD/ERCC2* was investigated in studies of lung ($n = 13$), breast ($n = 4$), bladder ($n = 4$), skin ($n = 7$), head and neck ($n = 2$), esophageal ($n = 2$), colorectal ($n = 1$), and prostate ($n = 1$) cancer, as well as glioma ($n = 1$) and leukemia ($n = 2$). *XRCC3* was investigated in studies of lung ($n = 7$), breast ($n = 5$), bladder ($n = 4$), and skin ($n = 5$) cancer and in single studies for each of the following types of cancer: leukemia, colorectal, endometrial, gastric, glioma, head and neck, and oral-larynx-pharynx. Many studies included evaluations of both genes. Occasionally, associations with cancers of the head and neck, prostate, endometrium, colon/rectum, or stomach or gliomas were described, but those studies were not included in the present meta-analysis. The association between lung cancer and *XPD* was considered in a previous HuGE review (9), but the current review has been updated (four more studies were included) and includes other cancers, as well as *XRCC3*.

STUDY DESIGNS

Web tables 2 and 3 (http://www.aje.oxfordjournals.org) describe the study designs for *XPD/ERCC2* and *XRCC3*, respectively. We identified 37 studies that examined the role of *XPD/ERCC2* and 28 studies that examined the role of *XRCC3*. Thirty-six studies were hospital-based case-control investigations, except for two case-cohort studies (one for each gene), two case-only studies, 14 population-based case-control studies for *XPD/ERCC2*, and nine population-based case-control studies for *XRCC3*. The majority of the studies were conducted in the United States (18 for *XPD/ERCC2*, 13 for *XRCC3*); others were from China, including Taiwan (six for *XPD/ERCC2*, two for *XRCC3*), Europe (26), South Korea (one for *XPD/ERCC2*), or Canada (one for *XRCC3*). In Western countries, mainly Caucasians were investigated, and the US studies often included African Americans.

Many studies included control for exposures such as smoking, alcohol drinking, occupation, and sunlight, but surprisingly, a number of investigators did not control for these important potential confounders. Data on the most studied exposures (smoking, alcohol, sunlight/sunburns) are reported in Web tables 2 and 3; for other exposures and exposures for which data were not available, findings are indicated as "null." Unfortunately, for most cancers, it has not been possible to conduct meta-analyses because of a lack of data stratified by exposure.

Smoking was investigated mainly in relation to lung cancer and bladder cancer. Tobacco smoking is the main known cause of both types of cancer, accounting for approximately 85–90 percent of lung cancers and 50 percent of bladder cancers occurring in Western populations (21). Ultraviolet light was investigated in relation to basal-cell carcinoma of the skin, as well as burns and skin type.

Genotypes for *XPD/ERCC2* and *XRCC3* were determined in virtually all studies through the use of polymerase chain reaction–restriction fragment length polymorphism or TaqMan (Applied Biosystems, Foster City, California). The latter has slightly greater sensitivity and specificity (22) than polymerase chain reaction–restriction fragment length polymorphism.

META-ANALYSIS

We conducted a search of the English literature using the National Library of Medicine's MEDLINE system and essential search terms for the years 1985 (January) to 2005 (March) to identify all published articles or abstracts in which the frequencies of *XPD* and *XRCC3* were determined for human cancer. (All of the Web tables and references to original papers are available on the ISI Foundation's Human Molecular Epidemiology website (http://www.hume.unito.it).) The search was organized by genetic polymorphism, organ site, histologic type, and any exposures evaluated as potential effect modifiers (i.e., exposures that may interact with genotype). We identified additional articles by searching through references cited in the first series of articles found in PubMed. Articles selected for meta-analysis were all case-control in design, had been published in the primary literature, and had no obvious overlap with each other in terms of subject. Heterogeneity among the studies was evaluated by means of Cochran's Q test (23) and was considered significant at $p < 0.05$. If the test result was negative, a fixed-effects model (Mantel-Haenszel method) was used. This model assumes a common genotype effect between the studies. On the contrary, if the test result was positive, we used a random-effects model (24) to take the heterogeneity into account. This model assumes that the studies are a random sample of a hypothetical population of studies taking into account within- and between-study variability. All of the calculations were performed with the computer program R, version 2.0.1 (R Foundation for Statistical Computing, Vienna, Austria).

Because heterogeneity of allele frequencies in different populations could have introduced bias into the odds ratio estimates if different ethnic groups had not been well-matched within studies, the quality of the studies used in our meta-analysis was carefully checked, as was control for potential bias. Nevertheless, ethnicity could have acted as an effect modifier if the odds ratios were significantly different in different populations. Thus, we repeated the meta-analysis, whenever possible, stratifying by population.

In order to include all possible studies (i.e., to increase the statistical power of the meta-analyses), we also used the absolute numbers calculated from published genotype frequencies in these studies. Thus, we performed the meta-analysis in two ways: first, based on the original odds ratios published in the papers (indicated as ''adjusted odds ratios''), and second, based on the absolute numbers reported in the papers or calculated from genotype frequencies and sample sizes (indicated as ''crude odds ratios'').

The wild type was defined on the basis of genotype frequencies (most common allele) unless functional information was available. When the analyses were both stratified (i.e., by another factor) and unstratified (i.e., considered the main genotype effect) in the same paper, we used the odds ratio based on the latter. We also used the crude odds ratio when ethnicity was not specified.

ASSOCIATIONS AND INTERACTIONS

XPD/ERCC2

Web table 4 shows the results of the meta-analyses for *XPD/ERCC2*. The study by Chen et al. (20) was excluded from the *XPD/ERCC2*-751 lung cancer meta-analysis because of the large difference in allele/genotype frequency between that population and other populations of the same ethnicity. A few statistically significant odds ratios were found. Codon 156 was important in skin cancer, and codons 312 and 751 were important in breast cancer and lung cancer. Codon 751 was also significant in esophageal squamous cell carcinoma, but only two studies were included in the meta-analysis, which produced a relatively wide 95 percent confidence interval. Tests for interstudy heterogeneity were not statistically significant for these associations; that is, results were consistent across studies. No significant associations were found for bladder cancer or leukemia. To test whether the heterogeneity of allele frequencies observed in different populations could have introduced bias into the odds ratio estimates for different ethnic groups, we performed meta-analyses by Asian and Caucasian ethnicity for *XPD/ERCC2*-751 and -312 in lung cancer (the only possible stratifications). The results showed that, for the above SNPs, there was no statistically significant difference in odds ratios between Asian and Caucasian populations, in spite of the different allele frequencies (Web table 1).

XRCC3

None of the odds ratios in meta-analyses of *XRCC3* were statistically significant (Web table 5 (http://www.aje.oxfordjournals.org)). However, the comparison between the TT and CC genotypes was close to statistical significance for lung cancer when the adjusted odds ratios were used (odds ratio = 1.25, 95 percent confidence interval: 0.97, 1.60). As for *XPD/ERCC2* meta-analyses, the interstudy heterogeneity test was negative. No stratification by ethnic group was possible for *XRCC3* polymorphisms.

DISCUSSION AND POPULATION TESTING

In spite of good biologic reasons for a role of DNA repair genetic polymorphisms in cancer risk modulation, the literature on the functional significance of the *XPD/ERCC2* and *XRCC3* genotypes considered remains relatively scanty (3). We chose two genes for which a reasonably large number of papers have been published and that are likely to be actively involved in both the repair of carcinogen adducts and the risk of cancer. We evaluated all cancer sites, because DNA repair is likely to take place in a rather nonspecific manner for different carcinogens and different cancers. However, with the accumulation of data on DNA repair gene polymorphisms, some SNPs seem to have opposite risk trends at different cancer sites. These results could simply reflect chance associations, although a possible explanation could be the tissue-specific balance between apoptotic signals and repair effects in the different tissues. Less efficient repair variants of specific repair pathways can result in a protective signal (accumulation of damage, cell-cycle block, apoptosis) in some tissues, whereas in others they could be risk factors (unrepaired or abortive attempt to repair damage and subsequent mutation).

For the most part, we found no association between the cancer sites we investigated and *XRCC3*. We detected some statistically significant associations between skin, breast, and lung cancers and *XPD/ERCC2* SNPs. These observations are not surprising, because *XPD/ERCC2* is known to play a key role in nucleotide excision repair, which in turn is crucial in, for example, the elimination of bulky DNA adducts. Less surprising is the lack of association with *XRCC3*. Potential explanations are both methodological (i.e., low study power to demonstrate small effects and too few cases to investigate disease heterogeneity (e.g., by tumor histology)) and substantive (i.e., the existence of multiple repair pathways that can compensate for each other). Moreover, our analysis did not consider the possibility of gene-gene or SNP-SNP interactions or the possibility of linkage disequilibrium between polymorphisms. Further investigations of the haplotypic effect of a gene and the study of multiple polymorphisms in different genes within the same pathway and different pathways are needed.

On the basis of our meta-analyses, there is no strong indication for testing populations, or subgroups with exposure to carcinogens, for the *XPD/ERCC2* or *XRCC3* genotype. However, given the many limitations of the existing literature mentioned above, more complete analyses of these genes are warranted. Although the evidence suggests that *XPD/ERCC2* could play a role in individual susceptibility to lung, breast, and skin cancer, the associations are weak and presently do not justify screening.

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Web Material
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Table 1 Genotype and allele frequencies.

***XRCC3*-IVS6 1571**

			Allele Freq (%)		Genotype Frequency (%)				Hardy-Weinberg
Study	**Year**	**Ethnicity**	**T**	**C**	**TT**	**TC**	**CC**	**N**	**p**
Jacobsen	2004	Caucasians	92.6	7.4	85.9	13.4	0.7	269	0.715

***XRCC3*-IVS5-14**

			Allele Freq (%)		Genotype Frequency (%)				
Study	**Year**	**Ethnicity**	**A**	**G**	**AA**	**AG**	**GG**	**N**	
Jacobsen	2004	Caucasians	63.7	36.3	40.1	47.2	12.7	269	0.735
Han	2004c	Mixed	64.1	36.0	41.6	44.9	13.5	659	0.521
Han	2004a	Undefined	69.5	30.5	48.0	43.0	9.0	1265	0.612

***XRCC3*-Cod.241**

			Allele Freq (%)		Genotype Frequency (%)				
Study	**Year**	**Ethnicity**	**C (Thr)**	**T (Met)**	**CC**	**CT**	**TT**	**N**	
David-Beabes	2001	African-Americans	76.9	23.1	58.1	37.6	4.3	234	0.372
Wang	2003	African-Americans	78.0	22.0	62.6	30.8	6.6	91	0.327
		African-Americans			**59.1**	**35.4**	**4.6**	**325**	
Shen	2004	Asians	95.3	4.9	90.4	9.7	0.0	166	0.500
Yeh	2005	Asians	94.8	5.4	89.7	10.1	0.3	736	0.855
		Asians			**89.8**	**10.0**	**0.2**	**902**	
Winsey	2000	Caucasians	70.5	29.5	52.0	37.0	11.0	211	0.109
Matullo	2001	Caucasians	63.0	37.0	49.0	28.0	23.0	85	**<0.001**
David-Beabes	2001	Caucasians	61.8	38.2	38.6	46.4	15.0	453	0.713
Seedhouse	2002	Caucasians	70.9	29.2	52.6	36.6	10.9	175	0.127
Duan	2002	Caucasians	61.2	38.9	36.4	49.5	14.1	319	0.455
Shen	2002	Caucasians	63.8	36.2	39.8	48.0	12.2	354	0.461
Jacobsen	2003	Caucasians	66.8	34.2	46.3	41.0	13.7	315	0.081
Jacobsen	2003	Caucasians	61.4	38.9	37.9	46.9	15.4	422	0.761
Misra	2003	Caucasians	71.0	29.0	49.0	44.0	7.0	315	0.224
Bertram	2004	Caucasians	64.0	36.0	40.0	48.0	12.0	335	0.446
Shen	2003	Caucasians	60.0	40.0	33.0	54.0	13.0	214	0.067
Sanyal	2004	Caucasians	66.0	34.0	44.0	44.0	12.0	246	0.758
Harms	2004	Caucasians	71.5	28.5	51.0	41.0	8.0	119	0.948
Wang	2004	Caucasians	64.5	35.5	43.0	43.0	14.0	342	0.259
Benhamou	2004	Caucasians	55.1	44.9	28.3	53.6	18.1	166	0.283

Jacobsen	2004	Caucasians	63.0	37.0	42.0	42.0	16.0	269	0.104
Smith	2003	Caucasians	62.8	35.3	38.7	48.1	11.2	268	0.218
		Caucasians			**41.4**	**44.9**	**12.4**	**4608**	
Wang	2003	Hispanic	77.8	22.2	62.6	30.3	7.1	99	0.220
Stern	2002	Mixed	67.0	33.0	45.0	44.0	11.0	209	0.943
David-Beabes	2001	Mixed	67.0	33.1	45.3	43.4	11.4	687	0.587
Smith	2003	Mixed	60.5	39.6	37.1	46.7	16.2	302	0.685
Wang	2003	Mixed	81.3	18.7	62.6	37.4	0.0	190	**0.002**
Han	2004b	Mixed	61.5	38.6	37.0	48.9	14.1	810	0.361
Han	2004c	Mixed	65.1	34.9	42.1	46.0	11.9	665	0.751
Han	2004a	Undefined	62.5	37.5	38.0	49.0	13.0	1245	0.110
Popanda	2004	Undefined	61.0	39.0	37.0	48.0	15.0	460	0.850
Figueiredo	2004	Undefined	61.2	38.8	36.3	49.8	13.9	402	0.330

***XRCC3*-A4552C**

			Allele Freq (%)		**Genotype Frequency (%)**				
Study	**Year**	**Ethnicity**	**A**	**C**	**AA**	**AC**	**CC**	**N**	
Han	2004	Mixed	81.0	19.1	65.5	30.9	3.6	861	0.956

***XRCC3*-5' region pos.4541**

			Allele Freq (%)		**Genotype Frequency (%)**				
Study	**Year**	**Ethnicity**	**A**	**G**	**AA**	**AG**	**GG**	**N**	
Winsey	2000	Caucasians	23.0	77.0	4.0	38.0	58.0	211	0.290
Jacobsen	2004	Caucasians	80.9	18.2	66.8	28.1	4.1	268	0.334
		Caucasians			**39.0**	**32.4**	**27.6**	**479**	
Han	2004c	Mixed	81.2	18.9	66.1	30.1	3.8	663	0.678
Han	2004a	Undefined	79.5	20.5	67.0	25.0	8.0	1291	**<<0.001**

***XPD/ERCC2*-Intron 4**

			Allele Freq (%)		**Genotype Frequency (%)**				
Study	**Year**	**Ethnicity**	**A**	**G**	**AA**	**AG**	**GG**	**N**	
Yin	2002	Caucasians	40.2	59.8	20.6	39.2	40.2	97	0.069

***XPD/ERCC2*-Cod.751**

			Allele Freq (%)		**Genotype Frequency (%)**				
Study	**Year**	**Ethnicity**	**C (Gln)**	**A (Lys)**	**CC**	**CA**	**AA**	**N**	
David-Beabes	2001	African-Americans	25.1	75.1	5.6	38.9	55.6	234	0.586

Stern	2002a	African -Americans	65.0	35.0	38.0	54.0	8.0	13	0.501
		African -Americans			**6.9**	**39.7**	**53.0**	**247**	
Park	2002	Asians	5.5	94.5	0.0	11.0	89.0	163	0.457
Xing	2002	Asians	7.3	92.8	0.6	13.3	86.1	524	0.800
Liang	2003	Asians	8.7	91.3	0.6	16.3	83.1	1010	0.494
Chen	2002	Asians	40.4	59.7	18.3	44.1	37.6	109	0.381
Xing	2002	Asians	7.2	92.8	0.8	12.8	86.4	383	0.409
Yu	2004	Asians	6.9	93.1	1.3	11.2	87.5	152	0.114
Yeh	2005	Asians	7.2	92.9	0.6	13.1	86.3	736	0.717
		Asians			**1.1**	**14.9**	**83.6**	**3077**	
Sturgis	2000	Caucasians	33.8	66.3	11.5	44.5	44.0	496	0.913
Dybdahl	1999	Caucasians	40.0	60.0	20.0	40.0	40.0	20	0.456
Winsey	2000	Caucasians	40.5	59.5	15.0	51.0	34.0	211	0.398
Spitz	2001	Caucasians	33.3	66.7	10.8	45.0	44.2	360	0.805
Vogel	2001	Caucasians	36.4	63.7	10.3	52.1	37.6	117	0.173
Matullo	2001	Caucasians	45.5	54.5	17.0	57.0	26.0	85	0.169
Caggana	2001	Caucasians	41.5	58.5	16.0	51.0	33.0	148	0.540
Stern	2002a	Caucasians	37.5	62.5	15.0	45.0	40.0	197	0.575
David-Beabes	2001	Caucasians	34.7	65.3	12.8	43.7	43.5	453	0.458
Seedhouse	2002	Caucasians	37.0	63.0	15.1	43.8	41.1	73	0.605
Misra	2003	Caucasians	40.5	59.5	15.0	51.0	34.0	315	0.302
Rybicki	2004	Caucasians	35.6	64.5	12.0	47.1	40.9	437	0.560
Shen	2003	Caucasians	40.0	60.0	17.0	46.0	37.0	214	0.542
Baccarelli	2004	Caucasians	42.7	57.3	18.7	48.0	33.3	177	0.800
Sanyal	2004	Caucasians	38.0	62.0	15.0	46.0	39.0	246	0.709
Harms	2004	Caucasians	27.5	72.5	6.0	43.0	51.0	119	0.393
Shi	2004	Caucasians	29.8	70.3	7.6	44.3	48.1	79	0.595
Allan	2004	Caucasians	36.5	63.5	15.0	43.0	42.0	729	0.051
Zhou	2002	Caucasians	36.0	63.0	13.0	46.0	40.0	1240	0.595
Justenhoven	2004	Caucasians	36.5	63.5	14.0	45.0	41.0	643	0.459
		Caucasians			**13.4**	**45.8**	**40.1**	**6359**	
David-Beabes	2001	Mixed	31.4	68.7	10.3	42.1	47.6	687	0.566
Buch	2005	Mixed	27.5	72.5	11.9	31.2	56.9	269	**<0.001**
Tang	2002	Undefined	36.4	63.6	17.4	38.0	44.6	121	**0.049**
Allan	2004	Undefined	36.5	63.5	15.0	43.0	42.0	729	0.051
Popanda	2004	Undefined	36.5	63.5	14.0	45.0	41.0	460	0.531
Terry	2005	Undefined	36.3	63.7	13.7	45.2	41.1	1102	0.453

***XPD/ERCC2*-Cod.711**

			Allele Freq (%)		Genotype Frequency (%)			
Study	**Year**	**Ethnicity**	**C (Asp)**	**T (Asp)**	**CC**	**CT**	**TT**	**N**

Caggana	2001	Caucasians	67.0	32.0	46.0	42.0	11.0	140	0.658

***XPD/ERCC2*-Cod.312**

			Allele Freq (%)		**Genotype Frequency (%)**				
Study	**Year**	**Ethnicity**	**G (Asp)**	**A (Asn)**	**GG**	**GA**	**AA**	**N**	
Xing	2002	Asians	93.9	6.1	88.0	11.8	0.2	524	0.492
Liang	2003	Asians	93.5	6.5	87.2	12.8	0.1	1020	0.083
Xing	2002	Asians	94.2	5.9	88.3	11.7	0.0	383	0.224
Yu	2004	Asians	94.8	5.3	89.5	10.5	0.0	152	0.495
		Asians			**87.7**	**12.0**	**0.0**	**2079**	
Winsey	2000	Caucasians	64.5	35.5	42.0	45.0	13.0	211	0.801
Spitz	2001	Caucasians	72.8	27.3	52.5	40.5	7.0	360	0.684
Butkiewicz	2001	Caucasians	56.5	43.5	31.0	51.0	18.0	96	0.713
Vogel	2001	Caucasians	62.4	37.7	43.8	37.1	19.1	105	**0.032**
Caggana	2001	Caucasians	64.5	35.5	41.0	47.0	12.0	137	0.758
Misra	2003	Caucasians	63.5	36.5	40.0	47.0	13.0	315	0.805
Rybicki	2004	Caucasians	66.2	33.9	41.2	49.9	8.9	437	**0.017**
Baccarelli	2004	Caucasians	60.2	39.9	34.3	51.7	14.0	172	0.304
Shi	2004	Caucasians	75.3	24.7	58.2	34.2	7.6	79	0.474
Zhou	2002	Caucasians	67.0	33.0	44.0	46.0	10.0	1240	0.156
Justenhoven	2004	Caucasians	66.0	34.0	45.0	42.0	13.0	610	0.113
		Caucasians			**43.5**	**45.1**	**11.1**	**3762**	
Tang	2002	Undefined	78.6	21.4	66.1	25.0	8.9	112	**0.007**
Popanda	2004	Undefined	63.5	36.5	42.0	43.0	15.0	460	0.121

***XPD/ERCC2*-Cod.156**

			Allele Freq (%)		**Genotype Frequency (%)**				
Study	**Year**	**Ethnicity**	**C (Arg)**	**A (Arg)**	**CC**	**CA**	**AA**	**N**	
Sturgis	2000	Caucasians	55.4	44.7	31.1	48.6	20.4	496	0.691
Dybdahl	1999	Caucasians	62.5	37.5	40.0	45.0	15.0	20	0.858
Winsey	2000	Caucasians	60.0	40.0	33.0	54.0	13.0	211	0.069
Vogel	2001	Caucasians	59.0	41.0	37.8	42.3	19.8	111	0.189
Caggana	2001	Caucasians	61.5	38.5	40.0	43.0	17.0	139	0.278
		Caucasians			**33.5**	**47.9**	**17.9**	**977**	

***XPD/ERCC2*-201**

			Allele Freq (%)		**Genotype Frequency (%)**			
Study	**Year**	**Ethnicity**	**C (His)**	**T (Tyr)**	**CC**	**CT**	**TT**	**N**
Sturgis	2002	Caucasians	100.0	0.0	100.0	0.0	0.0	400

***XPD/ERCC2*-199**

			Allele Freq (%)		Genotype Frequency (%)				
Study	**Year**	**Ethnicity**	**C (Ile)**	**G (Met)**	**CC**	**CG**	**GG**	**N**	
Sturgis	2002	Caucasians	99.2	0.9	98.3	1.7	0.0	400	0.864

Table 2. Study design: *XPD/ERCC2*

Study	Date	Nationality	Polymorphisms	Cancer Site	Method	Design	Ethnic group	No. case-controls	Exposure
Dybdahl	1999	Denmark	*XPD/ERCC2* Cod.751 *XPD/ERCC2* Cod.156	Skin	PCR-RFLP	H-B casecontrol	Caucasian	40/40	NULL
Sturgis	2000	USA	*XPD/ERCC2* Cod.751 *XPD/ERCC2* Cod.156	Head and neck	PCR-RFLP	H-B case-control	Non-Hispanic whites	189/496	Smoking, alcohol
Winsey	2000	UK	*XRCC1* Cod.399 *XPD/ERCC2* Cod.751 *XPD/ERCC2* Cod.156 *XRCC1* Cod.194 *XPD/ERCC2* Cod.312 *XPF/ERCC4* 5' UTR pos.2063 *XPF/ERCC4* Exon 11 pos.30028 *ERCC1* Exon 4 pos.19007 *XRCC3* Cod.241 *XRCC3* 5' region pos.4541	Skin	PCR-SSCP	H-B case control	Caucasians	125/211	NULL
Butkiewicz	2001	Poland	*XPD/ERCC2* Cod.312	Lung	PCR-RFLP	P-B case-control	Whites	96/96+52 members of 4 families	Smoking NULL
Caggana	2001	USA	*XPD/ERCC2* Cod.751 *XPD/ERCC2* Cod.156 *XPD/ERCC2* Cod.312 *XPD/ERCC2* Cod.711	Glioma	PCR-RFLP	P-B case control	Caucasian and Others	187/169	NULL
David-Beabes	2001	USA	*XPD/ERCC2* Cod.751 *XRCC3* Cod.241	Lung	PCR-RFLP	P-B case-control	Caucasians African Americans	331/687	NULL
Matullo	2001	Italy	*XRCC1* Cod.399 *XPD/ERCC2* Cod.751 *XRCC3* Cod.241	Bladder	PCR-RFLP	H-B case-control	Caucasians	124/85	Smoking
Spitz	2001	USA	*XPD/ERCC2* Cod.751 *XPD/ERCC2* Cod.312	Lung	PCR-RFLP HCRA	H-B case-control	Whites	341/360	Smoking,alcohol
Tomescu	2001	Scotland	*XPD/ERCC2* Cod.751 *XPD/ERCC2* Cod.156 *ERCC1* Exon 4 pos.19007 *XPD/ERCC2* Cod.711 *CKM* Exon 8 *CKM* 3'	Skin	PCR-RFLP	H-B case-control	Caucasians	28/28	NULL

Vogel	2001	USA	*XPD/ERCC2* Cod.751 *XPD/ERCC2* Cod.156 *XPD/ERCC2* Cod.312	Skin	PCR-RFLP	H-B case-control	Caucasians	70/117	Sunburns, skin type
Chen	2002	USA China	*XRCC1* Cod.399 *XPD/ERCC2* Cod.751 *XRCC1* Cod.194	Lung	PCR-RFLP	P-B case control	Asians	109/109	Smoking
Hou	2002	Sweden	*XPD/ERCC2* Cod.751 *XPD/ERCC2* Cod.312	Lung	PCR-RFLP	P-B case control	Undefined	185/162	Smoking
Park	2002	South Korea	*XPD/ERCC2* Cod.751	Lung	PCR-RFLP	H-B case-control	Asians	250/163	Smoking
Seedhouse	2002	UK	*XRCC1* Cod.399 *XPD/ERCC2* Cod.751 *XRCC1* Cod.194 *XRCC3* Cod.241 *NQO1* Cod. 187	Leukemia Secondary leukemia	PCR-RFLP	H-B case control	Caucasians	168/178	NULL
Stern	2002a	USA	*XPD/ERCC2* Cod.751	Bladder	PCR-RFLP	H-B case-control	Whites and blacks	228/210	Smoking
Sturgis	2002	USA	*XPD/ERCC2* 23047 *XPD/ERCC2* 23051	Head and neck	PCR-RFLP	H-B case control	Non-Hispanic whites	180/400	NULL
Tang	2002	USA	*XPD/ERCC2* Cod.751 *XPD/ERCC2* Cod.312	Breast	PCR-RFLP	H-B case control	Undefined	103/215	NULL
Xing	2002a	China	*XRCC1* Cod.399 *XPD/ERCC2* Cod.751 *XRCC1* Cod.194 *XPD/ERCC2* Cod.312	Esophageal	PCR-RFLP	P-B case control	Asians	433/524	Smoking
Xing	2002b	China	*XPD/ERCC2* Cod.751 *XPD/ERCC2* Cod.312	Lung	PCR-RFLP	P-B case control	Asians	351/383	Smoking
Yin	2002	Denmark	*XRCC1* Cod.399 *ERCC1* Exon 4 pos.19007 *CKM* Exon 8 *LIG1* exon 6 *XPD/ERCC2* Intron 4 *RAI* Exon 6 *RAI* Intron 1 *FOSB* Exon 4 *SLC1A5* Exon 8 *GLTSCR1* Exon 1	Skin	TaqMan	H-B case control	Caucasians	97/58	NULL
Zhou	2002	USA	*XPD/ERCC2* Cod.751	Lung	PCR-RFLP	P-B case control	Caucasians	1092/1240	Smoking

			XPD/ERCC2 Cod.312						
Gao	2003	USA	*XRCC1* Cod.399 *XPD/ERCC2* Cod.751 *XPD/ERCC2* Cod.312	Lung	TaqMan	Case-Only	Caucasians	204	Smoking
Liang	2003	China	*XPD/ERCC2* Cod.751 *XPD/ERCC2* Cod.312	Lung	PCR-RFLP	P-B case control	Asians	1006/1020	Smoking
Misra	2003	Finland	*XRCC1* Cod.399 *XPD/ERCC2* Cod.751 *XPD/ERCC2* Cod.312 *XRCC3* Cod.241 *XRCC1* Cod.280 *APEX* Cod. 148	Lung	TaqMan	P-B case control	Caucasians	315/315	Smoking
Shen	2003	USA Italy	*XRCC1* Cod.399 *XPD/ERCC2* Cod.751 *XRCC3* Cod.241	Bladder	PCR-RFLP	H-B case control	Caucasians	201/214	Smoking
Allan	2004	UK	*XPD/ERCC2* Cod.751	Leukemia	PCR-RFLP	P-B case control	Undefined	852/729	NULL
Baccarelli	2004	USA Italy	*XPD/ERCC2* Cod.751 *XPD/ERCC2* Cod.312	Skin	TaqMan	P-B case control	Caucasians	176/177	Sunlight
Brewster	2004	USA	*XPD/ERCC2* Cod.751	Skin	TaqMan	Case-cohort	Undefined	80/401	Smoking
Harms	2004	USA	*XRCC1* Cod.399 *XPD/ERCC2* Cod.751 *XRCC3* Cod.241	Lung	PCR-RFLP	H-B case control	Caucasians	110/119	Smoking
Justenhoven	2004	Germany	*XPD/ERCC2* Cod.751 *XPD/ERCC2* Cod.312	Breast	Sequencing	P-B case control	Caucasians	688/724	Smoking
Popanda	2004	Germany	*XRCC1* Cod.399 *XPD/ERCC2* Cod.751 *XPD/ERCC2* Cod.312 *XRCC3* Cod.241 *XPA* 5' NCR *APEX* Cod. 148	Lung	PCR-RFLP	H-B case control	Caucasians	463/460	Smoking
Rybicki	2004	USA	*XRCC1* Cod.399 *XPD/ERCC2* Cod.751 *XPD/ERCC2* Cod.312	Prostate	PCR-RFLP	P-B case control	Caucasians	637/480	NULL
Sanyal	2004	Sweden	*XRCC1* Cod.399 *XPD/ERCC2* Cod.751 *XRCC3* Cod.241	Bladder	TaqMan PCR-RFLP	H-B case control	Caucasians	327/246	NULL

			CCND1 Cod.870 *XPG* Cod. 1104 *NQO1* Exon 6 *NBS1* Cod. 185 *XPC* exon 4 *MTHFR* exon 4 *MTHFR* exon 7 *NQO1* exon 4 *H-ras* exon 1 *GSTT1* Deletion allele						
Shi	2004	USA	*XPD/ERCC2* Cod.751 *XPD/ERCC2* Cod.312	Breast	PCR-RFLP	H-B case control	Non-Hispanic whites	69/79	Smoking
Yu	2004	China	*XPD/ERCC2* Cod.751 *XPD/ERCC2* Cod.312	Esophageal	PCR-RFLP	H-B case control	Asians	135/152	Smoking Alcohol
Terry	2005	USA	*XPD/ERCC2* Cod.751	Breast	Other	P-B case control	Undefined	1053/1102	Smoking
Yeh	2005	Taiwan	*XRCC1* Cod.399 *XPD/ERCC2* Cod.751 *XRCC3* Cod.241	Colorectal	PCR-RFLP	H-B case control	Asians	727/736	NULL

Table 3. Study design: *XRCC3*

Study	Date	Nationality	Polymorphisms	Cancer Site	Method	Design	Ethnic group	Num. case-controls	Exposures
Winsey	2000	UK	*XRCC1* Cod.399 *XPD/ERCC2* Cod.751 *XPD/ERCC2* Cod.156 *XRCC1* Cod.194 *XPD/ERCC2* Cod.312 *XPF/ERCC4* 5' UTR pos.2063 *XPF/ERCC4* Exon 11 pos.30028 *ERCC1* Exon 4 pos.19007 *XRCC3* Cod.241 *XRCC3* 5' region pos.4541	Skin	PCR-SSCP	H-B case control	Caucasians	125/211	NULL
David-Beabes	2001	USA	*XPD/ERCC2* Cod.751 *XRCC3* Cod.241	Lung	PCR-RFLP	P-B case-control	Caucasians African Americans	331/687	Smoking
Matullo	2001	Italy	*XRCC1* Cod.399 *XPD/ERCC2* Cod.751 *XRCC3* Cod.241	Bladder	PCR-RFLP	H-B case-control	Caucasians	124/85	Smoking
Duan	2002	USA	*XRCC3* Cod.241	Skin	PCR-RFLP	H-B case control	Non-Hispanic whites	305/319	NULL
Seedhouse	2002	UK	*XRCC1* Cod.399 *XPD/ERCC2* Cod.751 *XRCC1* Cod.194 *XRCC3* Cod.241 *NQO1* Cod. 187	Leukemia Secondary leukemia	PCR-RFLP	H-B case control	Caucasians	168/178	NULL
Shen	2002	USA	*XRCC3* Cod.241	Head and neck	PCR-SSCP	H-B case control	Non-Hispanic whites	367/354	Smoking Alcohol
Stern	2002b	USA	*XRCC3* Cod.241	Bladder	PCR-RFLP	H-B case-control	White or black	233/209	Smoking
Jacobsen	2003	Denmark	*XRCC3* Cod.241	Breast Skin	PCR-RFLP Sequencing	H-B case control	Caucasians	319/321 426/424	NULL
Medina	2003	USA	*XRCC3* Cod.241 *BRCA2* Cod. 372 *NBS1* Cod. 185	Lung	PCR-RFLP	Case-Only	Caucasians African-Americans	109	NULL
Misra	2003	Finland	*XRCC1* Cod.399 *XPD/ERCC2* Cod.751 *XPD/ERCC2* Cod.312 *XRCC3* Cod.241	Lung	TaqMan	P-B case control	Caucasians	315/315	Smoking

			XRCC1 Cod.280 *APEX* Cod. 148						
Shen	2003	USA Italy	*XRCC1* Cod.399 *XPD/ERCC2* Cod.751 *XRCC3* Cod.241	Bladder	PCR-RFLP	H-B case control	Caucasians	201/214	Smoking
Smith	2003a	USA	*XRCC1* Cod.399 *XRCC1* Cod.194 *XRCC3* Cod.241	Breast	PCR-RFLP	P-B case control	Undefined	162/302	NULL
Smith	2003b	USA	*XRCC1* Cod.399 *XRCC1* Cod.194 *XRCC3* Cod.241 *XPF/ERCC4* Cod. 415	Breast	PCR-RFLP Sequencing	H-B case control	Undefined	253/268	NULL
Wang	2003	USA	*XRCC3* Cod.241	Lung	PCR-RFLP	P-B case control	African-Americans Mexican-Americans	112/190	Smoking
Benhamou	2004	France	*XRCC3* Cod.241 *XRCC2* Cod 188	Oral Pharynx Larynx	PCR-RFLP	H-B case control	Caucasians	250/172	Smoking
Bertram	2004	UK	*XRCC3* Cod.241	Skin	PCR-RFLP	P-B case control	Caucasians	140/335	NULL
Figueiredo	2004	Canada	*XRCC1* Cod.399 *XRCC3* Cod.241	Breast	Other	P-B case control	Undefined	402/402	Smoking Alcohol
Han	2004a	USA	*XRCC3* Cod.241 *XRCC3* 5' region pos.4541 *XRCC2* Cod 188 *XRCC3* IVS5-14 *LIG4* C299T *LIG4* Cod. 501	Breast	TaqMan	P-B case control	Undefined	1004/1385	NULL
Han	2004b	USA	*XRCC3* Cod.241 *XRCC2* Cod 188 *LIG4* C4062T *LIG4* C4044T *LIG4* Cod. 501 *XRCC2* C29244T *XRCC2* A31342G *XRCC2* G30833A *XRCC2* G30935A	Skin	TaqMan	P-B case control	Caucasians Asians Hispanics	805/873	NULL

			XRCC3 A4552C						
Han	2004c	USA	*XRCC3* Cod.241 *XRCC3* 5' region pos.4541 *XRCC2* Cod 188 *XRCC3* IVS5-14	Endometrial	TaqMan	H-B case control	Undefined	220/666	NULL
Harms	2004	USA	*XRCC1* Cod.399 *XPD/ERCC2* Cod.751 *XRCC3* Cod.241	Lung	PCR-RFLP	H-B case control	Caucasians	110/119	Smoking
Jacobsen	2004	Denmark	*XRCC3* Cod.241 *XRCC3* 5' region pos.4541 *XRCC3* IVS5-14 *XRCC3* IVS6 1571	Lung	TaqMan	Case-cohort	Caucasians	267/269	Smoking
Popanda	2004	Germany	*XRCC1* Cod.399 *XPD/ERCC2* Cod.751 *XPD/ERCC2* Cod.312 *XRCC3* Cod.241 *XPA* 5' NCR *APEX* Cod. 148	Lung	PCR-RFLP	H-B case control	Caucasians	463/460	Smoking
Sanyal	2004	Sweden	*XRCC1* Cod.399 *XPD/ERCC2* Cod.751 *XRCC3* Cod.241 *CCND1* Cod.870 *XPG* Cod. 1104 *NQO1* Exon 6 *NBS1* Cod. 185 *XPC* exon 4 *MTHFR* exon 4 *MTHFR* exon 7 *NQO1* exon 4 *H-ras* exon 1 *GSTT1* Deletion allele	Bladder	TaqMan PCR-RFLP	H-B case control	Caucasians	327/246	NULL
Shen	2004	China	*XRCC3* Cod.241	Gastric	PCR-RFLP	P-B case control	Asians	188/166	Smoking Alcohol
Wang	2004	USA	*XRCC1* Cod.399 *XRCC3* Cod.241	Glioma	PCR-RFLP	H-B case control	Caucasians	309/342	NULL

			TP53 Cod 72 *RAD51* 5` UTR *XRCC7* G6721T						
Yeh	2005	Taiwan	*XRCC1* Cod.399 *XPD/ERCC2* Cod.751 *XRCC3* Cod.241	Colorectal	PCR-RFLP	H-B case control	Asians	727/736	NULL

Table 4. Results: *XPD/ERCC2*

Cod.156 Skin

		CA vs CC				AA vs CC				CA + AA vs CC			
		OR	0.95	CI	weights	OR	0.95	CI	weights	OR	0.95	CI	weights
Adjusted OR	Dybdahl 1999 Caucasians	3.26	0.66	16.07	1.51	5.33	0.78	36.37	1.04				
Fixed effects meta-analysis	Vogel 2001 Caucasians	2.01	0.98	4.13	7.43	1.67	0.69	4.04	4.92				
	Summary	**2.18**	**1.13**	**4.20**		**2.05**	**0.92**	**4.56**					
	Heterogenity test X=	*0.29*				*1.16*							
	p-value=	*0.59*				*0.28*							
Crude OR	Dybdahl 1999 Caucasians	3.26	0.66	16.03	1.51	5.33	0.78	36.33	1.04	3.78	0.83	17.25	1.67
Fixed effects meta-analysis	Vogel 2001 Caucasians	2.01	0.98	4.14	7.39	1.67	0.69	4.04	4.92	1.90	0.96	3.76	8.28
	Winsey 2000 Caucasians	0.92	0.57	1.49	16.41	0.88	0.42	1.84	7.11	0.91	0.57	1.46	17.71
	Summary	**1.26**	**0.86**	**1.85**		**1.30**	**0.77**	**2.21**		**1.26**	**0.87**	**1.81**	
	Heterogenity test X=	*4.59*				*3.45*				*5.24*			
	p-value=	*0.10*				*0.18*				*0.07*			

Cod.312 Breast

		GA vs GG				AA vs GG				GA + AA vs GG			
		OR	0.95	CI	weights	OR	0.95	CI	weights	OR	0.95	CI	weights
Adjusted OR	Justenhoven 2004 Caucasians					0.49	0.33	0.72	24.47				
Random effects meta-analysis	Shi 2004 Caucasians					2.06	0.63	6.71	2.75	2.01	1.03	3.93	8.54
	Tang 2002 Undefined									1.58	0.85	2.94	9.92
	Summary					**0.89**	**0.22**	**3.63**		**1.77**	**1.12**	**2.79**	
	Heterogenity test X=					*5.17*				*0.27*			
	p-value=					*0.02*				*0.61*			
Crude OR	Justenhoven 2004 Caucasians	0.54	0.42	0.70	62.00	0.45	0.30	0.67	24.14	0.52	0.41	0.66	71.18
Random effects meta-analysis	Shi 2004 Caucasians	1.88	0.94	3.75	8.03	2.11	0.67	6.72	2.87	1.92	1.00	3.70	8.97
	Tang 2002 Undefined	1.58	0.85	2.93	9.93	1.00	0.36	2.79	3.63	1.42	0.80	2.52	11.71
	Summary	**1.12**	**0.46**	**2.74**		**0.87**	**0.34**	**2.23**		**1.08**	**0.44**	**2.65**	
	Heterogenity test X=	*18.29*				*7.39*				*21.01*			
	p-value=	*<0.01*				*0.02*				*<0.01*			

Cod.312 Lung

		GA vs GG				AA vs GG				GA + AA vs GG			
		OR	0.95	CI	weights	OR	0.95	CI	weights	OR	0.95	CI	weights

Adjusted OR	Liang 2003 Asians	1.03	0.80	1.32	61.82	10.33	1.29	82.61	0.89				
Fixed effects meta-analysis	Misra 2003 Caucasians	0.72	0.50	1.04	28.65	0.93	0.55	1.58	13.80				
	Popanda 2004 Undefined	1.14	0.83	1.56	39.39	1.05	0.68	1.62	20.69				
	Spitz 2001 Caucasians	0.93	0.63	1.38	24.54	1.51	0.76	3.00	8.15				
	Zhou 2002 Caucasians	0.98	0.80	1.20	93.47	1.41	1.10	1.80	63.36				
	Butkiewicz 2001 Caucasians					0.72	0.32	1.64	5.68				
	Summary	**0.98**	**0.86**	**1.11**		**1.25**	**1.04**	**1.51**					
	Heterogenity test X=	*3.84*				*8.74*							
	p-value=	*0.43*				*0.12*							
Crude OR	Butkiewicz 2001 Caucasians	0.50	0.26	0.94	9.47	0.74	0.33	1.66	5.85	0.56	0.31	1.01	11.04
Fixed effects meta-analysis	Liang 2003 Asians	0.98	0.76	1.28	55.66	11.24	1.45	87.25	0.91	1.06	0.82	1.37	57.93
	Misra 2003 Caucasians	0.74	0.53	1.04	33.87	0.93	0.57	1.52	16.14	0.78	0.57	1.07	38.45
	Popanda 2004 Undefined	1.15	0.87	1.52	48.90	1.07	0.72	1.58	25.19	1.13	0.87	1.46	55.56
	Spitz 2001 Caucasians	0.92	0.67	1.25	38.92	1.57	0.91	2.72	12.83	1.01	0.75	1.36	43.68
	Zhou 2002 Caucasians	1.00	0.84	1.19	127.42	1.47	1.12	1.92	53.73	1.08	0.92	1.28	142.23
	Summary	**0.96**	**0.86**	**1.07**		**1.30**	**1.08**	**1.55**		**1.02**	**0.92**	**1.13**	
	Heterogenity test X=	*8.26*				*10.13*				*7.87*			
	p-value=	*0.14*				*0.07*				*0.16*			

Cod.312 Skin

		GA vs GG				**AA vs GG**				**GA + AA vs GG**			
		OR	0.95	CI	weights	OR	0.95	CI	weights	OR	0.95	CI	weights
Adjusted OR	Baccarelli 2004 Caucasians									1.50	0.90	2.50	14.72
Fixed effects meta-analysis	Vogel 2001 Caucasians									1.05	0.57	1.94	10.24
	Summary									**1.30**	**0.88**	**1.92**	
	Heterogenity test X=									*0.77*			
	p-value=									*0.38*			
Crude OR	Baccarelli 2004 Caucasians	1.20	0.75	1.92	17.23	0.85	0.42	1.74	7.50	1.12	0.71	1.77	18.53
Fixed effects meta-analysis	Vogel 2001 Caucasians	1.02	0.51	2.02	8.21	1.11	0.49	2.54	5.63	1.05	0.57	1.94	10.12
	Winsey 2000 Caucasians	1.03	0.64	1.67	16.48	1.48	0.76	2.87	8.76	1.13	0.72	1.78	18.87
	Summary	**1.09**	**0.81**	**1.48**		**1.13**	**0.75**	**1.72**		**1.11**	**0.84**	**1.48**	
	Heterogenity test X=	*0.24*				*1.24*				*0.04*			
	p-value=	*0.89*				*0.54*				*0.98*			

Cod.751 Bladder

		CA vs AA				**CC vs AA**				**CA + CC vs AA**			
		OR	0.95	CI	weights	OR	0.95	CI	weights	OR	0.95	CI	weights
Adjusted OR	Sanyal 2004 Caucasians	1.07	0.73	1.57	26.20	1.31	0.77	2.22	13.71				

Fixed effects meta-analysis	Shen 2003 Caucasians	0.89	0.58	1.36	21.16	1.00	0.57	1.75	12.21	0.92	0.62	1.37	24.45
	Stern 2002b Caucasians	1.10	0.73	1.66	22.49	0.80	0.41	1.55	8.80				
	Matullo 2001 Caucasians									0.71	0.32	1.58	6.03
	Summary	**1.02**	**0.81**	**1.29**		**1.05**	**0.75**	**1.47**		**0.87**	**0.61**	**1.25**	
	Heterogenity test X=	*0.58*				*1.35*				*0.32*			
	p-value=	*0.75*				*0.51*				*0.57*			
Crude OR	Matullo 2001 Caucasians	0.76	0.40	1.43	9.40	0.75	0.31	1.77	5.14	0.75	0.41	1.39	10.17
Fixed effects meta-analysis	Sanyal 2004 Caucasians	1.08	0.75	1.56	28.27	1.29	0.78	2.12	15.47	1.13	0.80	1.60	32.06
	Shen 2003 Caucasians	0.89	0.58	1.36	21.14	1.01	0.58	1.77	12.34	0.92	0.62	1.37	24.31
	Stern 2002b Caucasians	1.05	0.69	1.59	21.79	0.85	0.46	1.55	10.53	1.00	0.67	1.48	24.45
	Summary	**0.98**	**0.78**	**1.21**		**1.02**	**0.76**	**1.37**		**0.99**	**0.80**	**1.21**	
	Heterogenity test X=	*1.19*				*1.70*				*1.44*			
	p-value=	*0.76*				*0.64*				*0.70*			

Cod.751 Breast

		CA vs AA				**CC vs AA**				**CA + CC vs AA**			
		OR	0.95	CI	weights	OR	0.95	CI	weights	OR	0.95	CI	weights
Adjusted OR	Justenhoven 2004 Caucasians	1.09	0.85	1.39	63.53	1.32	0.94	1.86	32.99				
Fixed effects meta-analysis	Shi 2004 Caucasians	1.41	0.71	2.82	8.00	1.49	0.46	4.84	2.76	1.19	0.62	2.30	8.82
	Tang 2002 Undefined	1.03	0.58	1.84	11.32	1.02	0.45	2.30	5.80				
	Terry 2005 Undefined	1.22	1.01	1.47	113.17	1.18	0.91	1.53	56.92	1.21	1.01	1.44	122.14
	Summary	**1.17**	**1.02**	**1.35**		**1.22**	**1.00**	**1.49**		**1.21**	**1.02**	**1.43**	
	Heterogenity test X=	*0.98*				*0.56*				*<0.01*			
	p-value=	*0.81*				*0.90*				*0.96*			
Crude OR	Justenhoven 2004 Caucasians	1.08	0.85	1.38	64.43	1.32	0.94	1.84	34.03	1.14	0.90	1.43	73.22
Fixed effects meta-analysis	Shi 2004 Caucasians	1.12	0.57	2.22	8.30	1.69	0.53	5.40	2.85	1.20	0.63	2.31	9.12
	Tang 2002 Undefined	1.10	0.62	1.95	11.59	0.91	0.43	1.96	6.63	1.04	0.61	1.76	13.72
	Terry 2005 Undefined	1.20	1.00	1.44	114.39	1.18	0.91	1.54	55.73	1.20	1.01	1.42	127.76
	Summary	**1.15**	**1.00**	**1.32**		**1.22**	**1.00**	**1.48**		**1.17**	**1.02**	**1.33**	
	Heterogenity test X=	*0.50*				*1.10*				*0.33*			
	p-value=	*0.92*				*0.78*				*0.95*			

Cod.751 Esophageal Squamous cell carcinoma

		CA vs AA				**CC vs AA**				**CA + CC vs AA**			
		OR	0.95	CI	weights	OR	0.95	CI	weights	OR	0.95	CI	weights

Crude OR	Xing 2002a Asians	1.11	0.77	1.60	28.49	1.23	0.25	6.12	1.49	1.11	0.77	1.59	29.59
Fixed effects meta-analysis	Yu 2004 Asians	1.09	0.52	2.28	7.03	7.39	1.62	33.73	1.67	1.75	0.92	3.32	9.39
	Summary	**1.10**	**0.79**	**1.53**		**3.62**	**1.30**	**10.06**		**1.24**	**0.91**	**1.70**	
	Heterogenity test X=	*<0.01*				*2.59*				*1.47*			
	p-value=	*0.97*				*0.11*				*0.23*			

Cod.751 Leukemia

		CA vs AA				CC vs AA				CA + CC vs AA			
		OR	0.95	CI	weights	OR	0.95	CI	weights	OR	0.95	CI	weights
Adjusted OR	Allan 2004 Caucasians	1.20	0.91	1.58	51.66	1.22	0.84	1.78	27.25				
Fixed effects meta-analysis	Seedhouse 2002 Caucasians	0.74	0.31	1.77	5.06	0.61	0.18	2.05	2.61				
	Summary	**1.15**	**0.89**	**1.49**		**1.15**	**0.80**	**1.64**					
	Heterogenity test X=	*1.08*				*1.14*							
	p-value=	*0.30*				*0.28*							
Crude OR	Allan 2004 Caucasians	1.18	0.91	1.53	55.88	1.18	0.82	1.68	29.75	1.18	0.92	1.51	63.56
Fixed effects meta-analysis	Seedhouse 2002 Caucasians	1.20	0.63	2.28	9.16	1.09	0.44	2.69	4.72	1.17	0.64	2.15	10.36
	Summary	**1.18**	**0.93**	**1.51**		**1.16**	**0.83**	**1.62**		**1.18**	**0.94**	**1.48**	
	Heterogenity test X=	*<0.01*				*0.02*				*<0.01*			
	p-value=	*0.97*				*0.88*				*0.98*			

Cod.751 Lung

		CA vs AA				CC vs AA				CA + CC vs AA			
		OR	0.95	CI	weights	OR	0.95	CI	weights	OR	0.95	CI	weights
Adjusted OR	David-Beabes 2001 African-Americans	1.08	0.66	1.76	15.97	1.03	0.40	2.65	4.30	1.07	0.67	1.71	17.50
Fixed effects meta-analysis	David-Beabes 2001 Caucasians	0.97	0.62	1.52	19.11	1.34	0.74	2.42	10.95	1.06	0.70	1.61	22.15
	Harms 2004 Caucasians	1.39	0.79	2.44	12.08	0.95	0.26	3.45	2.31	1.33	0.77	2.30	12.73
	Liang 2003 Asians	0.95	0.74	1.22	61.48	2.71	1.01	7.26	3.96				
	Misra 2003 Caucasians	0.82	0.56	1.20	27.05	1.02	0.61	1.70	14.63	0.87	0.61	1.24	31.24
	Popanda 2004 Undefined	1.16	0.85	1.59	39.18	1.39	0.90	2.14	20.48				
	Spitz 2001 Caucasians	1.07	0.78	1.47	38.26	1.36	0.84	2.20	16.58				
	Zhou 2002 Caucasians	1.01	0.87	1.17	185.67	1.17	0.91	1.51	58.89				
	Xing 2002b Asians									1.42	0.94	2.15	22.45
	Summary	**1.02**	**0.92**	**1.12**		**1.24**	**1.05**	**1.47**		**1.09**	**0.91**	**1.32**	
	Heterogenity test X=	*3.60*				*3.96*				*3.68*			
	p-value=	*0.82*				*0.78*				*0.45*			

Crude OR	David-Beabes 2001 African-Americans	1.14	0.74	1.74	21.18	1.39	0.59	3.26	5.31	1.17	0.78	1.76	23.00
Fixed effects meta-analysis	David-Beabes 2001 Caucasians	1.14	0.78	1.68	26.29	1.72	1.04	2.86	15.00	1.27	0.89	1.82	30.38
	Harms 2004 Caucasians	1.32	0.77	2.24	13.48	1.05	0.33	3.31	2.89	1.28	0.76	2.16	14.28
	Liang 2003 Asians	0.93	0.73	1.19	66.60	2.34	0.89	6.11	4.16	0.98	0.78	1.24	70.16
	Misra 2003 Caucasians	0.87	0.62	1.23	32.09	1.09	0.68	1.74	17.24	0.92	0.66	1.28	35.77
	Popanda 2004 Undefined	1.14	0.86	1.51	48.39	1.36	0.92	2.01	25.37	1.19	0.91	1.55	54.78
	Spitz 2001 Caucasians	1.07	0.78	1.46	38.33	1.36	0.84	2.20	16.58	1.12	0.83	1.51	42.81
	Xing 2002b Asians	1.33	0.88	2.01	22.51	1.91	0.45	8.06	1.85	1.37	0.91	2.04	23.90
	Zhou 2002 Caucasians	1.03	0.86	1.22	123.31	1.19	0.92	1.53	59.98	1.06	0.90	1.25	138.25
	Summary	**1.05**	**0.95**	**1.16**		**1.31**	**1.11**	**1.54**		**1.10**	**1.00**	**1.21**	
	Heterogenity test X=	*4.72*				*4.20*				*4.78*			
	p-value=	*0.86*				*0.84*				*0.85*			

Cod.751 Skin

		CA vs AA				**CC vs AA**				**CA + CC vs AA**			
		OR	0.95	CI	weights	OR	0.95	CI	weights	OR	0.95	CI	weights
Adjusted OR	Baccarelli 2004 Caucasians									1.30	0.67	2.54	8.59
Random effects meta-analysis	Dybdahl 1999 Caucasians					0.23	0.04	1.26	1.33				
	Vogel 2001 Caucasians					1.83	0.71	4.70	4.31	1.18	0.64	2.18	10.15
	Summary					**0.74**	**0.10**	**5.51**		**1.23**	**0.78**	**1.94**	
	Heterogenity test X=					*4.35*				*0.04*			
	p-value=					*0.04*				*0.83*			
Crude OR	Baccarelli 2004 Caucasians	1.12	0.71	1.79	17.67	0.74	0.39	1.40	9.42	1.02	0.65	1.58	19.55
Fixed effects meta-analysis	Dybdahl 1999 Caucasians	0.90	0.24	3.41	2.17	0.20	0.02	2.16	0.68	0.67	0.19	2.33	2.45
	Vogel 2001 Caucasians	1.05	0.55	2.01	9.14	1.83	0.71	4.70	4.33	1.18	0.64	2.19	10.06
	Winsey 2000 Caucasians	0.75	0.46	1.22	16.00	1.13	0.59	2.14	9.29	0.84	0.53	1.32	18.29
	Summary	**0.95**	**0.71**	**1.27**		**0.98**	**0.66**	**1.45**		**0.96**	**0.73**	**1.26**	
	Heterogenity test X=	*1.50*				*4.33*				*1.17*			
	p-value=	*0.68*				*0.23*				*0.76*			

Table 5. Results: *XRCC3*

Cod.241 Bladder

		CT vs CC				TT vs CC				CT + TT vs CC			
		OR	0.95	CI	weights	OR	0.95	CI	weights	OR	0.95	CI	weights
Adjusted OR	Sanyal 2004 Caucasians	0.97	0.66	1.42	26.67	1.31	0.75	2.27	12.64				
fixed effects meta-analysis	Shen 2003 Caucasians	0.60	0.40	0.90	22.74	0.74	0.39	1.39	9.62	0.63	0.42	0.94	24.32
	Stern 2002b Mixed	1.20	0.78	1.85	20.54	1.50	0.82	2.76	10.39				
	Matullo 2001 Caucasians									2.72	1.37	5.42	8.10
	Summary	**0.88**	**0.70**	**1.12**		**1.16**	**0.82**	**1.63**		**1.27**	**0.30**	**5.33**	
	Heterogenity test X=	*5.56*				*2.82*				*13.00*			
	p-value=	*0.06*				*0.24*				*<0.01*			
Crude OR	Matullo 2001 Caucasians	3.50	1.81	6.75	8.90	1.77	0.85	3.71	7.04	2.71	1.51	4.87	11.26
Random effects meta-analysis	Sanyal 2004 Caucasians	0.93	0.64	1.33	29.37	1.42	0.85	2.38	14.51	1.03	0.74	1.45	33.76
	Shen 2003 Caucasians	0.60	0.39	0.91	21.88	0.69	0.37	1.30	9.72	0.62	0.41	0.92	24.11
	Stern 2002b Mixed	1.24	0.83	1.84	24.05	1.48	0.81	2.72	10.48	1.28	0.88	1.88	26.80
	Summary	**1.19**	**0.66**	**2.12**		**1.26**	**0.93**	**1.70**		**1.18**	**0.71**	**1.95**	
	Heterogenity test X=	*20.91*				*4.81*				*18.02*			
	p-value=	*<0.01*				*0.19*				*<0.01*			

Cod.241 Breast

		CT vs CC				TT vs CC				CT + TT vs CC			
		OR	0.95	CI	weights	OR	0.95	CI	weights	OR	0.95	CI	weights
Adjusted OR	Figueiredo 2004 Undefined	0.96	0.70	1.31	39.96	1.44	0.94	2.20	21.48				
fixed effects meta-analysis	Han 2004a Undefined	0.87	0.72	1.05	107.95	0.98	0.75	1.28	53.78				
	Jacobsen 2003 Caucasians	1.01	0.75	1.36	44.48	0.89	0.59	1.35	22.43				
	Summary	**0.92**	**0.80**	**1.06**		**1.04**	**0.86**	**1.27**					
	Heterogenity test X=	*0.80*				*3.01*							
	p-value=	*0.67*				*0.22*							
Crude OR	Figueiredo 2004 Undefined	0.98	0.72	1.33	40.95	1.44	0.95	2.19	22.28	1.08	0.81	1.44	45.97
Fixed effects meta-analysis	Han 2004a Undefined	0.85	0.71	1.02	115.55	1.00	0.76	1.30	54.44	0.88	0.74	1.05	128.93
	Jacobsen 2003 Caucasians	1.01	0.75	1.35	44.72	0.89	0.59	1.35	22.36	0.98	0.74	1.29	49.99
	Smith 2003b Caucasians	0.88	0.60	1.29	26.80	1.84	1.08	3.13	13.70	1.06	0.75	1.52	30.55
	Smith 2003a Mixed	0.95	0.62	1.44	21.90	0.96	0.54	1.69	11.92	0.95	0.64	1.41	24.80
	Summary	**0.91**	**0.80**	**1.03**		**1.11**	**0.94**	**1.33**		**0.95**	**0.85**	**1.07**	
	Heterogenity test X=	*1.24*				*7.04*				*1.89*			
	p-value=	*0.87*				*0.13*				*0.76*			

Cod.241 Lung

		CT vs CC				TT vs CC				CT + TT vs CC			
		OR	0.95	CI	weights	OR	0.95	CI	weights	OR	0.95	CI	weights
Adjusted OR	David-Beabes 2001 African-Americans	0.90	0.55	1.48	15.68	1.67	0.57	4.88	3.34	0.98	0.61	1.57	17.43
fixed effects meta-analysis	David-Beabes 2001 Caucasians	0.93	0.60	1.44	20.37	0.94	0.50	1.75	9.92	0.93	0.62	1.40	22.76
	Harms 2004 Caucasians	0.66	0.36	1.19	10.90	1.25	0.47	3.32	4.02	0.75	0.43	1.30	12.55
	Jacobsen 2004 Caucasians	1.54	1.05	2.26	26.15	1.46	0.87	2.46	14.11				
	Misra 2003 Caucasians	0.96	0.69	1.34	34.88	1.12	0.59	2.12	9.39	1.14	0.62	2.11	10.17
	Popanda 2004 Undefined	0.95	0.69	1.31	37.39	1.29	0.85	1.97	21.49				
	Summary	**1.00**	**0.85**	**1.18**		**1.25**	**0.97**	**1.60**		**0.93**	**0.73**	**1.20**	
	Heterogenity test X=	*7.19*				*1.56*				*1.05*			
	p-value=	*0.21*				*0.91*				*0.79*			
Crude OR Fixed effects meta-analysis	David-Beabes 2001 African-Americans	0.93	0.60	1.43	20.68	1.36	0.53	3.48	4.36	0.97	0.64	1.47	22.45
	David-Beabes 2001 Caucasians	0.86	0.59	1.24	27.43	0.81	0.47	1.39	13.29	0.84	0.59	1.20	30.99
	Harms 2004 Caucasians	0.76	0.43	1.32	12.47	1.20	0.48	2.98	4.63	0.83	0.49	1.40	14.26
	Jacobsen 2004 Caucasians	1.29	0.89	1.88	27.51	1.05	0.63	1.76	14.5	1.51	1.06	2.16	30.10
	Misra 2003 Caucasians	0.87	0.63	1.20	35.93	1.22	0.67	2.22	10.65	0.91	0.67	1.25	39.36
	Popanda 2004 Undefined	0.87	0.65	1.16	47.36	1.23	0.84	1.80	26.72	0.96	0.73	1.25	54.06
	Summary	**0.92**	**0.79**	**1.07**		**1.11**	**0.88**	**1.39**		**0.99**	**0.86**	**1.14**	
	Heterogenity test X=	*4.12*				*1.92*				*6.94*			
	p-value=	*0.53*				*0.86*				*0.23*			

Cod.241 Skin

		CT vs CC				TT vs CC				CT + TT vs CC			
		OR	0.95	CI	weights	OR	0.95	CI	weights	OR	0.95	CI	weights
Crude OR Random effects meta-analysis	Bertram 2004 Caucasians	1.12	0.72	1.72	20.58	1.47	0.80	2.72	10.21	1.19	0.79	1.79	22.90
	Duan 2002 Caucasians	0.91	0.65	1.28	33.21	0.82	0.50	1.36	15.25	0.89	0.65	1.23	36.59
	Winsey 2000 Caucasians	2.35	1.44	3.84	15.89	2.58	1.28	5.16	7.95	2.40	1.51	3.82	17.77
	Summary	**1.31**	**0.77**	**2.23**		**1.41**	**0.74**	**2.71**		**1.34**	**0.77**	**2.33**	
	Heterogenity test X=	*9.77*				*7.06*				*11.73*			
	p-value=	*0.01*				*0.03*				*<0.01*			